

WE CLAIM:

1. A method of detecting thermal infrared radiation, comprising:

providing a sample substrate having a plurality of discrete sample sites configured

5 to support a corresponding plurality of samples;

providing an optical device configured preferentially to detect thermal infrared radiation;

detecting thermal infrared radiation transmitted from a sample positioned at a corresponding sample site using the optical device;

10 converting the detected thermal infrared radiation to a signal; and

processing the signal to reduce noise by replacing at least a portion of the signal with a revised portion formed from distinguishable components of the signal representing thermal infrared radiation detected from the same position in the sample at different times or from different positions in the sample at the same time.

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2. The method of claim 1, further comprising correlating the processed signal with the progress of a chemical or physiological reaction occurring in the sample.

3. The method of claim 1, where the sample sites keep at least a portion of each sample from mixing with at least a portion of each other sample.

4. The method of claim 1, where the sample substrate is a microarray.

5. The method of claim 1, where the sample sites keep each portion of each sample from mixing with each portion of each other sample.

6. The method of claim 1, where the sample substrate is a microplate, and  
5 where the sample sites are microplate wells.

7. The method of claim 1, where the number of sample sites is selected from the group consisting of 96, 384, 768, 1536, 3456, and 9600.

8. The method of claim 1, where the density of sample sites is at least about 1  
10 well per 81 mm<sup>2</sup>.

9. The method of claim 1, where the optical device comprises:  
an examination site; and  
15 a detector configured to receive and preferentially to detect thermal infrared radiation transmitted from a sample positioned at a sample site at the examination site.

10. The method of claim 1, further comprising shielding the sample from incident radiation to reduce the proportion of the signal arising from transmission,  
20 reflection, and/or photoluminescence from the sample.

11. The method of claim 1, further comprising filtering the radiation transmitted from the sample to extract thermal infrared radiation prior to the step of detecting thermal infrared radiation.

5 12. The method of claim 1, where at least about half of the thermal infrared radiation detected by the optical device has a wavelength between about 3 micrometers and about 5 micrometers.

10 13. The method of claim 1, where at least about half of the thermal infrared radiation detected by the optical device has a wavelength between about 7 micrometers and about 14 micrometers.

15 14. The method of claim 1, where the processed signal is representative of the temperature of the sample.

20 15. The method of claim 1, where the revised portion is formed from distinguishable components of the signal representing thermal infrared radiation detected from the same position in the sample at different times and from different positions in the sample at the same time.

16. The method of claim 1, where the revised portion is formed from distinguishable components of the signal representing thermal infrared radiation detected from the same position in the sample at different times and not from different positions in the sample at the same time.

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17. The method of claim 1, where the revised portion is formed from distinguishable components of the signal representing thermal infrared radiation detected from different positions in the sample at the same time and not from the same position in the sample at different times.

18. The method of claim 1, where the revised portion is formed for at least one position in the sample from distinguishable components of the signal from at least four different times.

15 19. The method of claim 18, where the revised portion is formed for at least one position in the sample from distinguishable components of the signal from at least sixteen different times.

20 20. The method of claim 1, where the revised portion is formed for at least one time from distinguishable components of the signal from at least four different positions in the sample.

21. The method of claim 18, where the revised portion is formed for at least one time from distinguishable components of the signal from at least nine different positions in the sample.

5 22. The method of claim 1, where the step of processing is adapted preferentially to reduce high-frequency temporal noise in the signal.

23. The method of claim 1, where the step of processing is adapted preferentially to reduce high-frequency spatial noise in the signal.

24. The method of claim 1, where the step of processing the signal includes the step of forming a weighted average of distinguishable components of the signal representing thermal infrared radiation detected from the same position in the sample at different times.

15 25. The method of claim 1, where the step of processing the signal includes the step of forming a weighted average of distinguishable components of the signal representing thermal infrared radiation detected from different positions in the sample at the same time.

26. The method of claim 1, the revised portion being formed from distinguishable components of the signal representing thermal infrared radiation detected from the same sample at different times, further comprising re-processing the signal by replacing at least a portion of the revised portion of the signal with a re-revised portion formed from distinguishable components of the revised portion representing thermal infrared radiation detected from the same sample at different times, where the times used to process the signal and the times used to re-process the signal may be the same or different.

27. The method of claim 1, where the signal is an image, and where the step of processing the signal includes forming a frame-average of a plurality of images.

28. The method of claim 1, where the signal comprises a set of discrete data points, and where the step of processing the signal reduces the number of data points.

29. The method of claim 1, further comprising:

detecting thermal infrared radiation transmitted from a reference region adjacent the sample site; and

constructing a sample signal characteristic of the thermal infrared radiation detected from the sample based on the processed signal and the thermal infrared radiation detected from the reference region.

30. The method of claim 29, the sample sites having a central axis, where the thermal reference region includes an annular emissive reference surface positioned about the central axis of each sample site.

5 31. The method of claim 29, where the thermal reference region has an emissivity of at least about 0.5.

10 32. The method of claim 29, further comprising repeating the steps of detecting thermal infrared radiation transmitted from a sample and detecting thermal infrared radiation transmitted from an adjacent reference region for a plurality of samples positioned at a corresponding plurality of the sample sites associated with the sample plate.

15 33. The method of claim 1, further comprising covering the sample wells to reduce evaporative heat loss from the samples.

20 34. The method of claim 1, further comprising repeating the steps of detecting, converting, and processing for a plurality of samples positioned at a corresponding plurality of the sample sites associated with the sample substrate.

35. The method of claim 34, where the thermal infrared radiation is detected simultaneously from the plurality of samples.

36. The method of claim 34, where the thermal infrared radiation is detected sequentially from the plurality of samples.

37. The method of claim 34, further comprising adjusting the processed signal  
5 corresponding to each sample so that each processed signal has the same preselected value at the same preselected time.

38. The method of claim 37, where the preselected value is zero.

39. The method of claim 37, where the preselected time is zero.

40. The method of claim 34, further comprising displaying the processed signals graphically in a manner representative of the arrangement of the corresponding sample sites on the substrate.

41. The method of claim 34, where the processed signal comprises a single value for each sample at each time.



42. A system for detecting thermal infrared radiation, comprising:

a sample substrate having a plurality of discrete sample sites configured to support a corresponding plurality of samples;

an optical device having an examination site and a detector, where the optical  
5 device is configured preferentially to detect thermal infrared radiation transmitted from a  
sample positioned at a corresponding sample site at the examination site; and

a processor incorporating instructions for and capable of carrying out the function of reducing noise by replacing at least a portion of the signal with a revised portion formed from distinguishable components of the signal representing thermal infrared radiation detected from the same position in the sample at different times or from different positions in the sample at the same time.

43. A system for detecting thermal infrared radiation, comprising:

means for supporting a plurality of samples at a corresponding plurality of discrete  
15 sample sites;

means for preferentially detecting thermal infrared radiation transmitted from a sample positioned at a corresponding sample site; and

means for reducing noise by replacing at least a portion of the signal with a revised portion formed from distinguishable components of the signal representing thermal infrared radiation detected from the same position in the sample at different times or from different positions in the sample at the same time.